

CLAIMS

What is claimed is:

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1. A method for determining whether a biomolecule produces a phenotypic effect on a cell, comprising the steps of:
- a) introducing into an animal a cell comprising an exogenous regulable gene encoding the biomolecule;
- b) regulating expression of the gene to produce the biomolecule in the cell; and
- c) monitoring said cell in the animal for a phenotypic effect;
- 10 whereby a cell which manifests a phenotypic effect indicates that the biomolecule produced in the cell is a biomolecule that produces a phenotypic effect on the cell.
2. The method of Claim 1 wherein the biomolecule is a peptide.
3. The method of Claim 1 wherein the phenotypic effect is inhibition of growth.
- 15 4. The method of Claim 3 wherein the cell is a pathogen cell.
5. The method of Claim 3 wherein the cell is a mammalian cell.
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6. A method for determining whether a biomolecule produces a phenotypic effect on a cell, comprising the steps of:
- a) constructing a cell comprising an exogenous regulable gene encoding the biomolecule;
- b) introducing said cell into an animal;
- c) regulating expression of the gene to produce the biomolecule in the cell; and

d) monitoring said cell in the animal for a phenotypic effect;
whereby a cell which manifests a phenotypic effect indicates that the
biomolecule produces a phenotypic effect on the cell.

5 7. A method for determining whether a biomolecule is a biomolecular inhibitor of
growth of cells, comprising:

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- 10 a) introducing into one or more test animals and into one or more suitable
control animals cells having a regulable gene encoding a biomolecule;
b) regulating, in the test animals, expression of the gene to allow production
of the biomolecule; and
c) monitoring said test animals for growth of the cells;
wherein observing fewer cells or a slower growth rate of the cells in said test
animals compared to the number of cells or growth rate in suitable control
animals indicates that the biomolecule is a biomolecular inhibitor of growth of
cells.

15 8. A method for assessing whether a biomolecule is a biomolecular inhibitor of
growth of cells in a host mammal comprising:
a) constructing cells having a regulable gene encoding the biomolecule;
b) introducing the cells into test animals and into suitable control animals;
c) regulating, in the test animals, expression of the regulable gene to
20 produce the biomolecule; and
d) monitoring the test animals and control animals for growth of the cells;
wherein observing less growth of the cells in test animals than in the control
animals indicates that the biomolecule is a biomolecular inhibitor of growth of
cells.

25 9. The method of Claim 8 wherein the cells are cells of a pathogenic organism.

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10. The method of Claim 8 wherein the cells are mammalian cells.

11. A method for determining whether a target component of a cell is essential for normal growth of said cell, comprising:

- a) in cells comprising a biomolecule and a target cell component, wherein the biomolecule is a biomolecular binder of the target cell component, and wherein a gene encoding the biomolecule is regulable, regulating expression of the gene to produce the biomolecule;
- b) monitoring growth of the cells in culture relative to growth of suitable control cells, whereby, if growth is decreased in the cells compared to growth of suitable control cells, then the biomolecule is a biomolecular inhibitor of growth;
- c) introducing into one or more test animals cells in which growth can be decreased compared to the control cells as determined in step b);
- d) regulating expression of the gene to produce the biomolecular inhibitor of growth in the introduced cells; and
- e) monitoring said test animals for inhibition of the growth of the cells; wherein observing fewer cells or slower growth of cells in said test animals compared to cells or growth of cells, respectively, in suitable control animals indicates that the target component of said cell is essential for normal growth of said cell.

12. A method for identifying a biomolecular inhibitor of growth of cells, comprising:

- a) in cells comprising a biomolecule and a target cell component, wherein the biomolecule is a biomolecular binder of the target cell component, and the gene encoding the biomolecule is regulable, regulating expression of the gene to allow production of the biomolecule;

- 5 b) monitoring growth of the cells in culture relative to growth of suitable control cells, whereby, if growth is decreased in the cells compared to growth of suitable control cells, then the biomolecule is a biomolecular inhibitor of growth;
- 10 c) introducing into one or more test animals cells in which growth can be decreased compared to the control cells in step b);
- 15 d) regulating expression of the gene to allow production of the biomolecule in the introduced cells; and
- 20 e) monitoring said test animals for inhibition of the growth of the cells; wherein observing fewer cells or slower growth of cells in said test animals compared to cells or growth of cells, respectively, in suitable control animals indicates that the biomolecule is a biomolecular inhibitor of infection.
- 25 13. A method for identifying a compound which is a functional analog of a biomolecule which produces a phenotypic effect on a cell, said method comprising the steps of:
- 15 a) testing, for the phenotypic effect, a cell which produces a biomolecule by regulable expression of an exogenous gene in the cell; and
- 20 b) identifying, if the biomolecule caused the phenotypic effect, one or more compounds that compete with the biomolecule for binding to a target cell component, whereby if a compound competes with the biomolecule for binding to the target cell component, then the compound is a functional analog of a biomolecule which produces a phenotypic effect on the cell.
14. The method of Claim 13 wherein the biomolecule is a peptide.
15. The method of Claim 13 wherein the phenotypic effect is inhibition of growth.
- 25 16. The method of Claim 15 wherein the cell is a pathogen cell.

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17. The method of Claim 15 wherein the cell is a mammalian cell.
18. A method for identifying a compound which is a functional analog of a biomolecule which produces a phenotypic effect on a cell, said method comprising the steps of:
- 5 a) constructing a cell comprising an exogenous gene which regulably produces the biomolecule;
- b) testing the cell in culture for the phenotypic effect, upon production of the biomolecule; and
- 10 c) identifying, if the phenotypic effect is observed upon production of the biomolecule, one or more compounds that compete with the biomolecule for binding to a target cell component, whereby if a compound competes with the biomolecule for binding to the target cell component, then the compound produces a phenotypic effect on the cell.
19. The method of Claim 18 wherein the biomolecule is a peptide.
- 15 20. The method of Claim 18 wherein the phenotypic effect is inhibition of growth.
21. The method of Claim 20 wherein the cell is a pathogen cell.
22. The method of Claim 20 wherein the cell is a mammalian cell.
23. A method for identifying a compound which produces a phenotypic effect in a cell, said method comprising the steps of:
- 20 a) constructing a cell comprising an exogenous regulable gene which encodes a biomolecule;
- b) introducing said cell into an animal;
- c) regulating expression of the gene to produce the biomolecule in the cell;

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- 5 d) monitoring said cell in the animal for the phenotypic effect; and
e) identifying, if the biomolecule caused the phenotypic effect, one or more compounds that competitively bind to a target cell component, whereby if the compound competitively binds to the target cell component, then the compound produces the phenotypic effect.

24. The method of Claim 23 wherein the biomolecule is a peptide.
25. The method of Claim 23 wherein the phenotypic effect is inhibition of growth.
26. The method of Claim 25 wherein the cell is a pathogen cell.
27. The method of Claim 25 wherein the cell is a mammalian cell.
- 10 28. A method for determining whether a biomolecule produces a phenotypic effect on a first cell, comprising:
a) identifying a biomolecule which binds to an isolated target cell component of the first cell;
b) constructing a second cell comprising the target cell component and a regulable, exogenous gene encoding the biomolecule; and
15 c) testing the second cell for the phenotypic effect, upon production of the biomolecule in the second cell;
whereby, if the second cell shows the phenotypic effect upon production of the biomolecule, then the biomolecule produces a phenotypic effect on the first cell.
- 20 29. The method of Claim 28 wherein the biomolecule is a peptide.
30. The method of Claim 28 wherein the phenotypic effect is inhibition of growth.

31. The method of Claim 30 wherein the cell is a pathogen cell.
32. The method of Claim 30 wherein the cell is a mammalian cell.
33. A method for determining whether a target component of a first cell is essential to producing a phenotypic effect on the first cell, comprising:
- 5 a) isolating the target component of the first cell;
- b) identifying a biomolecular binder of the isolated target component of the first cell;
- c) constructing a second cell comprising the target component and a regulable, exogenous gene encoding the biomolecular binder; and
- 10 d) testing the second cell in culture for an altered phenotypic effect, upon production of the biomolecular binder in the second cell;
- whereby, if the second cell shows the altered phenotypic effect upon production of the biomolecular binder, then the target component of the first cell is essential to producing the phenotypic effect on the first cell.
- 15 34. The method of Claim 33 wherein the phenotypic effect is normal growth rate.
35. A method for determining whether a biomolecule produces a phenotypic effect on a first cell, comprising:
- a) identifying a biomolecular binder of an isolated target cell component of the first cell;
- 20 b) constructing a second cell comprising the target cell component and a regulable, exogenous gene encoding the biomolecular binder; and
- c) testing the second cell in culture for the phenotypic effect, upon production of the biomolecular binder in the second cell;

whereby, if the second cell shows the phenotypic effect upon production of the biomolecular binder, then the biomolecule produces a phenotypic effect on the first cell.

36. The method of Claim 35 wherein the biomolecule is a peptide.

5 37. The method of Claim 35 wherein the phenotypic effect is inhibition of growth.

38. The method of Claim 37 wherein the cell is a pathogen cell.

39. The method of Claim 37 wherein the cell is a mammalian cell.

40. A method for identifying one or more compounds that produce a phenotypic effect on a cell, said method comprising the steps of:

- 10 a) identifying a biomolecular binder of an isolated target cell component of said cell;
- b) constructing a second cell in which an exogenous gene encoding said biomolecular binder is regulably expressed;
- 15 c) testing said second cell for the phenotypic effect upon expression of the gene encoding the biomolecular binder; and
- d) identifying, if the biomolecular binder caused the phenotypic effect in the second cell, one or more compounds that compete with the biomolecular binder for binding to the target cell component in a competitive binding assay;

20 whereby, if a compound competes with the biomolecular binder for binding to the target cell component, then the compound produces a phenotypic effect on said cell.

41. The method of Claim 40 wherein the biomolecule is a peptide.

42. The method of Claim 40 wherein the phenotypic effect is inhibition of growth.
43. The method of Claim 42 wherein the cell is a pathogen cell.
44. The method of Claim 42 wherein the cell is a mammalian cell.
45. A method for identifying one or more compounds that produce a phenotypic effect on a cell, said method comprising the steps of:
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- a) identifying a biomolecular binder of an isolated target cell component of said cell;
 - b) constructing a second cell in which an exogenous gene encoding said biomolecular binder is regulably expressed;
 - 10 c) testing said second cell in culture for the phenotypic effect upon expression of the gene encoding the biomolecular binder; and
 - d) identifying, if the biomolecular binder caused the phenotypic effect in the second cell, one or more compounds that compete with the biomolecular binder for binding to the target cell component in a competitive binding assay;
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- whereby, if a compound competes with the biomolecular binder for binding to the target cell component, then the compound produces a phenotypic effect on said cell.
46. The method of Claim 45 wherein the biomolecule is a peptide.
- 20 47. The method of Claim 45 wherein the phenotypic effect is inhibition of growth.
48. The method of Claim 47 wherein the cell is a pathogen cell.
49. The method of Claim 47 wherein the cell is a mammalian cell.

50. A method for determining whether a biomolecule produces a phenotypic effect on a first cell, comprising:
- a) identifying a biomolecular binder of an isolated target cell component of the first cell;
 - b) constructing a second cell comprising the target cell component and an exogenous, regulable gene which encodes the biomolecular binder;
 - c) introducing the second cell into one or more animals;
 - d) regulating expression of the gene, thereby producing the biomolecule in the second cell;
 - e) monitoring the second cell in the animal(s) for the phenotypic effect; and
 - f) identifying, if the biomolecular binder caused the phenotypic effect in the second cell, one or more compounds that compete with the biomolecular binder for binding to the target cell component;
- whereby, if a compound competes with the biomolecular binder for binding to the target cell component, then the compound produces the phenotypic effect on the first cell.
51. The method of Claim 50 wherein the biomolecule is a peptide.
52. The method of Claim 50 wherein the phenotypic effect is inhibition of growth.
53. The method of Claim 52 wherein the cell is a pathogen cell.
54. The method of Claim 52 wherein the cell is a mammalian cell.
55. A method for identifying a biomolecular inhibitor of growth of cells of a pathogen comprising:
- a) contacting a biomolecule with isolated target cell component of the pathogen;

- b) applying a means of detecting bound complexes of biomolecules and target cell component, whereby, if said bound complexes are detected, the biomolecule has been identified as a biomolecular binder of the target cell component;
- 5 c) constructing a pathogen having a regulable gene encoding the biomolecular binder;
- d) regulating expression of the gene encoding the biomolecular binder, thereby expressing the gene; and
- 10 e) monitoring growth of cells of the pathogen in culture relative to suitable control cells;
- whereby, if growth of the cells of the pathogen is decreased compared to growth of suitable control cells, then the biomolecule(s) is a biomolecular inhibitor of growth of the pathogen cells.

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A method for identifying one or more compounds that bind to a target cell component in a pathogen and inhibit infection of a mammal by the pathogen comprising:

- a) constructing a pathogen comprising a regulable gene encoding a biomolecule which binds to the target cell component;
- b) infecting one or more test animals with the constructed pathogen;
- 20 c) regulating expression of the regulable gene to produce the biomolecule;
- d) monitoring the test animals and one or more suitable control animals for signs of infection, wherein observing fewer or less severe signs of infection in the test animals than in the control animals indicates that the biomolecule is a biomolecular inhibitor of infection; and
- 25 e) identifying one or more compounds that compete with the biomolecular inhibitor of infection for binding to the target cell component in a competitive binding assay;

whereby, if a compound competes with the biomolecular inhibitor of infection for binding to the target cell component, then the compound binds to a target cell component in a pathogen and inhibits infection of a mammal by the pathogen.

57. A method for identifying one or more compounds that bind to a target cell component in a pathogen and inhibit infection of a mammal by the pathogen, comprising:
- a) constructing a pathogen comprising a regulable gene encoding a biomolecule which binds to the target cell component;
 - b) regulating expression of the gene in a culture of constructed pathogen cells, thereby producing the biomolecule in the constructed pathogen cells;
 - c) monitoring growth of the constructed pathogen cells in culture, relative to growth of suitable control cells, whereby, if growth is decreased in the constructed pathogen cells, compared to growth of the control cells, then the biomolecule is a biomolecular inhibitor of growth;
 - d) infecting one or more test animals with the constructed pathogen;
 - e) regulating expression of the regulable gene, thereby producing the biomolecule;
 - f) monitoring the test animals and the control animals for signs of infection, wherein observing fewer or less severe signs of infection in the test animals than in the control animals indicates that the biomolecule is a biomolecular inhibitor of infection; and
 - g) identifying one or more compounds that compete with the biomolecular inhibitor of infection for binding to the target cell component;
- whereby, if a compound competes with the biomolecular inhibitor of infection for binding to the target cell component, then the compound binds to the target cell component in the pathogen and inhibits infection of the mammal by the pathogen.

58. A method for identifying a biomolecular inhibitor of infection, comprising:
- a) in pathogen cells comprising a biomolecule and a cell component, wherein the biomolecule is a biomolecular binder of the cell component, and expression of the gene encoding the biomolecule is regulable, regulating expression of the gene, thereby producing the biomolecule;
 - b) monitoring growth of the pathogen cells in culture relative to growth of the control cells, whereby, if growth is decreased in the pathogen cells compared to growth of the control cells, then the biomolecule is a biomolecular inhibitor of growth;
 - c) infecting one or more test animals with the pathogen cells in which growth was decreased compared to the control cells in step b);
 - d) regulating expression of the gene, thereby producing the biomolecule; and
 - e) monitoring said test animals for signs of infection;
- wherein observing fewer or less severe signs of infection in said test animals compared to signs of infection in suitable control animals indicates that the biomolecule is a biomolecular inhibitor of cell growth.

59. Pathogen cells comprising a biomolecule and a target cell component, wherein the biomolecule is produced by expression of a regulable gene, and wherein the biomolecule inhibits function of said cell component, thereby causing a decrease in growth rate of said pathogen cells.

60. The pathogen cells of Claim 59 wherein the pathogen is fungal.

61. The pathogen cells of Claim 59 wherein the pathogen is a parasite.

62. The pathogen cells of Claim 59 wherein the pathogen is a yeast.

63. The pathogen cells of Claim 59 wherein the pathogen is bacterial.
64. Pathogen cells comprising a biomolecule and a target cell component, wherein the biomolecule is a biomolecular binder of the target cell component, and is encoded by a regulable gene.
- 5 65. The pathogen cells of Claim 64 ^B wherein regulation of the gene encoding the biomolecule to allow expression of the regulable gene causes a decrease in growth rate of the cells.
66. The pathogen cells of Claim 64 wherein the target cell component is of unknown function.

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